

Applicants: Iva Greenwald and Diane Levitan
Serial No.: Not Yet Known
Filed: Herewith
Page 9

REMARKS

Claims 1-86 are pending. Claims 1-46, and 50-86 have been canceled without prejudice. Claims 47-49 have been amended to more particularly point out what applicants regard as the invention. Support for these amendments is found *inter alia* in the specification in the Third Series of Experiments beginning at page 50. Applicants maintain that this amendment raises no issue of new matter. Thus, upon entry of this Preliminary Amendment, claims 47-49 will be pending and under examination.

The present invention provides a method for determining whether an agent increases presenilin activity comprising introducing the agent to a transgenic *Caenorhabditis elegans* animal, wherein the animal exhibits an egg-laying defective (*Egl*) phenotype induced by partial or total loss of SEL-12 protein activity, and determining whether the agent rescues the *Egl* phenotype, such rescue indicating that that agent increases presenilin activity. This invention is based, in part, upon applicants' surprising discovery that the *C. elegans* SEL-12 protein and human presenilins PS1 and PS2 are functional homologs (see page 50, lines 5-7). Thus, as demonstrated by the Third Series of Experiments beginning at page 50 of the specification, the human presenilins can rescue an egg laying defect ("Egl") caused by reduced SEL-12 activity (see also Table 4 at page 56 and Table 5 at page 60). The present invention provides an assay in which an agent is tested for its ability to rescue the *Egl* phenotype, such rescue indicating that the agent increases presenilin activity.